continuing need for the discovery of novel agents that are effective to ameliorate the symptoms of this condition.

Antigen activates the release of mediators of ocular allergy from the mast cells found in the eye. Histamine is one of these mediators, which is present in the secretory granules of mast cells and basophils and is formed by decarboxylation of histidine.

Histamine has been implicated in the redness and itching found in seasonal eye allergy. Anti-histamine compounds that bind to histamine receptors in the eye have been found to be useful in treating the signs and symptoms of eye allergy. Most of these drugs are compounds that are structurally related to histamine and bind to its receptor(s), thereby obstructing the interaction of histamine with its receptor(s). However, the drugs that are currently available often have undesirable side effects (for example drowsiness) and are not always effective.

Conventional H_1 receptor antagonists are widely used as antihistamine agents for treating allergic reactions including allergic rhinitis (hay fever), urticaria, insect bites and drug hypersensitivities. H_1 receptor antagonists target the redness and inflammation that is associated with these conditions. However, there are numerous undesirable effects of the H_1 receptor antagonists currently used. When used for purely antihistamine actions, all of the effects on the central nervous system (CNS) are unwanted. When used for their sedative or anti-emetic actions, some of the CNS effects such as dizziness, tinnitus and fatigue are unwanted. Excessive doses can cause excitation and may produce convulsions in children. The peripheral anti-muscarinic actions are always undesirable. The commonest of these is dryness of the mouth, but blurred vision, constipation and retention of urine can also occur. Unwanted effects not related to the drug's pharmaceutical action are also seen. Thus, gastrointestinal disturbances are fairly common while allergic dermatitis can follow topical application of these drugs.

H_2 receptor antagonists are also used as anti-histamine agents. These agents target the itching that is associated with the condition as a result of activation of certain aspects of the nervous system.

In addition to the problems mentioned above, some histamine antagonists are troublesome if taken with alcohol or with drugs. For example, the antihistamine Seldane used in combination with antibiotics and antifungals may cause life-threatening side-effects.

Preferably, the histacalin protein is derived from a blood-feeding ectoparasite, such as a leech, mosquito or tick. Most preferably, the histacalin protein is derived from a tick, in particular a species of hard tick such as *R. appendiculatus*, *I . ricinus* and *D. reticulatus*.

The histacalin proteins described above may be used for the treatment of any conjunctivitis condition. Preferably, they are used for the treatment of non-infective conjunctivitis, more preferably allergic conjunctivitis. In particular, the term allergic conjunctivitis is meant to include seasonal and perennial conjunctivitis, as well as vernal keratoconjunctivitis, giant papillary conjunctivitis and atopic keratoconjunctivitis.

The histacalin proteins as defined in above, particularly in section (e), can be used as diagnostic tools in the evaluation of the disease state of a patient who is suspected of suffering from non-infective conjunctivitis.

Any mammalian subject is suitable for treatment by the method of the present invention. Preferably, the patient is human.

Preferably, a pharmaceutically-acceptable carrier is also used in the manufacture of the medicament according to the invention. Such a pharmaceutically-acceptable carrier is also preferably used in the method of the present invention.

Suitable pharmaceutically-acceptable carriers include carriers that do not themselves induce the production of antibodies that are harmful to the individual receiving the composition. Typically, suitable carriers are large, slowly metabolised macromolecules such as proteins, polysaccharides, polylactic acids, polyglycolic acids, polymeric amino acids, amino acid copolymers, lipid aggregates (such as oil droplets or liposomes) and inactive virus particles. Such carriers are well known to those of skill in the art.

Pharmaceutically-acceptable carriers in therapeutic compositions may also contain liquids such as water, saline, glycerol and ethanol. Additionally, auxiliary substances, such as wetting or emulsifying agents and pH buffering substances, may be present. The compositions may be prepared as injectables, either as liquid solutions or suspensions. Solid forms suitable for solution or suspension in liquid vehicles prior to injection may also be prepared. Preparations for oral administration may be formulated to allow for controlled release of the active agent.

Optionally, one or more other, conventional antihistamine agents or anti-sedative agents may also be used in the manufacture of the medicament according to the invention.

μg/kg or, more typically, between 0.05 μg/kg and 10 μg/kg of the individual to which it is administered. Preferably, for topical administration to the eye, the histacalin proteins are present in solution at between 0.1% and 20%, more preferably between 1% and 10%. A suitable unit dose may range between 0.1μg and 1mg, preferably between 1μg and 200μg, more preferably between 10μg and 100μg for each eye. A unit dose of 96μg to each eye has been found effective.

Various aspects and embodiments of the present invention will now be described in more detail by way of example with reference to the accompanying drawings in which:

Figure 1 shows the mean change from baseline redness scores following pre-treatment of rabbit eyes with either 1% EV131 (HBP) or saline;

Figure 2 shows the mean change from baseline redness scores following pre-treatment of rabbit eyes with either 6% EV131 (HBP) or saline;

Figure 3 shows the mean change from baseline redness scores following pre-treatment of rabbit eyes with either 10% EV131 (HBP) or saline;

Figure 4 shows the mean change from baseline chemosis scores following pre-treatment of rabbit eyes with either 6% EV131 (HBP) or saline; and

Figure 5 shows the mean change from baseline chemosis scores following pre-treatment of rabbit eyes with either 10% EV131 (HBP) or saline.

Figure 6 shows the mean change from baseline redness scores following one week loading with either 6% EV131 or saline and then challenge with 48/80 8 hours following dosing.

It will be appreciated that modification of detail may be made without departing from the scope of the invention.

EXAMPLE 1

In this study, the irritability and efficacy of various concentrations of an ophthalmic solution of a histacalin protein have been evaluated in a compound 48/80 model of mast cell degranulation in the rabbit.

Compound 48/80 is the condensation product of N-methyl-p-methoxyphenethylamine with formaldehyde, and promotes the release of allergy mediators, including histamine, from the mast cell. Due to its pro-inflammatory actions,

Compound 48/80 has been used to screen new anti-allergic compounds in animals (Udell *et al.*, Am. J. Ophthalmol., 91, (2), 226-230, 1981).

In the present study, Compound 48/80 was used to determine the efficacy of the histacalin protein FS-HBP2 as described in PCT/GB97/01372 (herein referred to by its internal designation "EV131" and in the Figures by the designation "HBP") in preventing the signs of allergic conjunctivitis.

EV131 ophthalmic solution was prepared in 1% and 6% concentrations from stock that contained approximately 2 mg EV131 and 50 microliters dH_20. Physiological saline, pH 7.2, was used as the buffer to make the dilutions.

Treatment was with either saline, or with 1%, 6% or 10% EV131 using the rabbit model. Each rabbit was topically dosed in the right eye with 40 microliters EV131 solution, and in the left eye with 40 micoliters saline.

Rabbits were given a baseline gross examination for hyperaemia, chemosis, mucous discharge and lid swelling. One rabbit that showed an abnormal examination (>+1 hyperaemia and corneal changes) was excluded from the study.

Five rabbits were dosed with 1% EV131 and four rabbits were dosed with 6% EV131. Ten minutes following dosing, 25 microliters of a 7.5 mg/ml of a solution of Compound 48/80 (Sigma Chemical Co., St. Louis, MO, USA) was topically instilled in the pre-dosed eyes.

All rabbits were examined by gross examination at 3 min, 5 min, 10 min, 20 min, 60 min, 8 hours and 24 hours following challenge with Compound 48/80. Eyes were evaluated for conjunctival injection, chemosis, tearing, mucous discharge and lid swelling.

A dose of 6% (97μg) EV131 was found to give optimum results of consistent reduction in inflammation as measured by hyperaemia, chemosis, mucous discharge and lid swelling.

After a three week refractory period, the procedure was repeated. This time, four rabbits were dosed with 6% EV131 and five rabbits were dosed with 10% EV131.

One rabbit in the 6% HBP group had mucus in both eyes. Three rabbits in the 6% group (1 rabbit at 20, 60 and 240 minutes post-challenge and 2 rabbits at 60 minutes post-challenge) had mucus only in the placebo pre-treated eye. In the 10% treated group, 1 rabbit only had mucus in the EV131 treated eye (60 minutes and 8 hours post-challenge)